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“Groovy” Plastic Helps Rebuild Nerves

Thin polymer film provides direction for nerve cell growth

It takes a powerful microscope to actually see what Surya Mallapragada has developed, but its impact could be huge, especially for millions of people with various forms of paralysis. Micrographs showing tiny nerve cells growing along in an orderly fashion demonstrate how important this breakthrough could be in the ability to rewire broken nerve circuits in the human body.

Mallapragada's technique uses microscale channels cut in an ultrathin, biodegradable polymer to regrow nerve cells. The method has already been proven to work for peripheral

nerve regeneration in laboratory rats, and it may one day allow the paralyzed to walk and the blind to see.

Nerve cells are unlike most other biological tissue. When a nerve is severed, the part of the neuron “downstream” of the injury typically dies off. And neurons in the human body can be several feet long. Grafting, which works well for other tissue, such as skin, isn't the best option because it's difficult to get the nerve cells to line up and reconnect. There's also a loss of nerve function where the donor tissue is removed.

“Nerve cells aren't able to easily bridge gaps of more than one centimeter,” says Mallapragada, *continued on next page*



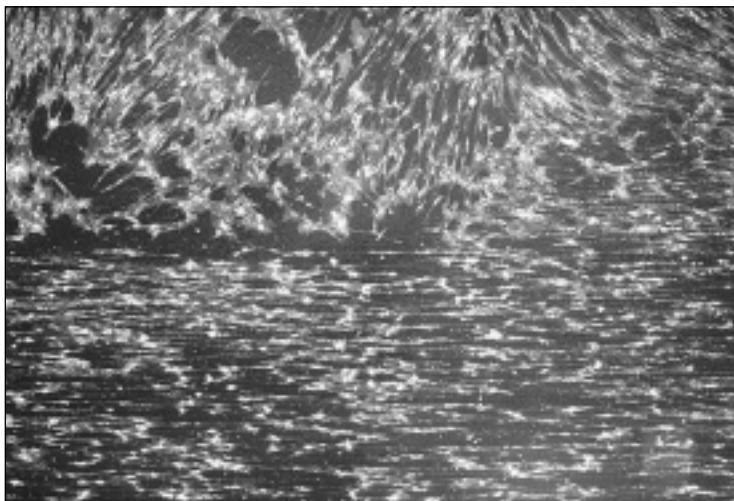
Ames Lab associate scientist Surya Mallapragada prepares to load a sample in an atomic force microscope in the Roy J. Carver Laboratory for Ultrahigh Resolution Biological Microscopy. She has used this type of microscope to make nanoscale grooves in a thin polymer film.

“Groovy” plastic helps rebuild nerves

continued from page 1

an Ames Laboratory associate in both the Environmental and Protection Sciences and Materials Chemistry programs, and a chemical engineering professor at Iowa State University. “Peripheral nervous system (PNS) axons

right direction. Starting with biodegradable polymer films only a few hundred microns thick (100 microns equals 0.004 in. — significantly less than the thickness of a human hair), Mallapragada and her colleagues



A micrograph shows nerve cells aligned with grooves in the bottom half and growing randomly in the smooth-surfaced top half.

— the part of the nerve cell which carries the impulses — normally have a connective tissue sheath of myelin to guide their growth, and without that guidance, they aren’t able to grow productively. They tend to branch out and form in knots.”

Since the nervous system carries electrical impulses, it helps to think of nerve cells in terms of electrical wiring. Bundles of nerves are like an electrical cable with multiple wires. When a nerve “cable” is cut and cells die, it would be as though the copper wire downstream of the damage disappeared, leaving only the empty plastic insulation tubes. In order for new copper wiring to push out across the gap and fill in the empty insulation tubes, you’d need a way to guide the wires into the empty tubes. And that’s where Mallapragada’s research comes in.

By working on a cellular scale, she has developed a way to help guide neurons so they grow in the

have developed methods for making minute patterns on these incredibly thin materials.

“We’ve made grooves three to four microns deep to help channel nerve cell growth,” Mallapragada says. “The grooves have a protein coating and we’ve also ‘seeded’ them with Schwann cells to help promote this growth.” Schwann cells naturally form the myelin sheath around the PNS cells. When guided by this sheath, nerves will grow at a rate of three to four millimeters per day.

The polymers, primarily poly(lactide-co-glycolide) and polyanhydrides, degrade when exposed to water, and Mallapragada has worked to develop thin film polymers that bulk degrade in layers over a period of time, ranging from a few days to almost a year. To put the microscale grooves in the polymers, she has used both laser etching and reactive ion etching, relying on the Ames Lab’s Environmental and

Protection Sciences Program and the Microanalytical Instrumentation Center’s Carver and Keck Laboratories for the necessary equipment and expertise.

After promising *in vitro* tests, Mallapragada worked with collaborators at Iowa State University’s College of Veterinary Medicine to conduct trials on rats. Small segments of the rats’ sciatic nerves, which deliver nerve messages to the hind legs, were removed and the severed nerves “spliced” using the polymer film. Though initially unable to use their legs, the rats started to regain use of their legs after three weeks and were able to function normally after six weeks.

Although the technique has shown great promise with PNS cell growth, getting similar results with the central nervous system, which includes the brain, spinal cord and optic nerve, is another matter. CNS cells grow differently than peripheral nerves, presenting special problems. Oligodendrocytes, the connective tissue of the CNS, can actually inhibit nerve growth. Mallapragada has focused the next phase of her research on the optic nerve to try to better understand how CNS neurons work and grow.

“There are other factors at work, such as chemical and electrical cues,” Mallapragada says. “Other researchers have had some success injecting adult (rat) stem cells into the site of the damaged optic nerve. Our hope is to eventually develop arrays of microelectrodes that will allow us to interface the optic nerve with a retinal chip — a bioartificial optic nerve, if you will.”

The retinal chip, first developed at Johns Hopkins University, uses chip technology to replace the eye’s rods and cones. The technology transfers the digital images to the optic nerve via

electrodes, but it is limited by the inability to create electrodes that are small enough and numerous enough to create a resolution sufficient for the brain to decipher the input as it does with normal “sight.”

“This research is a strong step forward in our basic understanding of nerve cell growth and how to engineer materials that help the body repair itself,” says Ari Patrinos, Director of the Department of Energy’s Office of Biological and Environmental Research. “We hope the groundwork laid by Ames Laboratory will soon pave the way for human subjects to benefit from this technology.”

Mallapragada was honored for this and related polymer research in 2002 by being named one of the world’s top 100 young innovators by *Technology Review*, a technology magazine published by the Massachusetts Institute of Technology. She is also associate director of the Microanalytical Instrumentation Center at Iowa State University. ■

~ Kerry Gibson